IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Docket No.:

Serial No.: Group Art Unit:

Filing Date: Examiner:

For:

DECLARATION OF SHERMAN FONG, Ph.D. UNDER 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Sherman Fong, Ph.D. declare and say as follows: -

1. I was awarded a Ph.D. in Microbiology by the University of California at Davis, CA in 1975.

2. After postdoctoral training and holding various research positions at Scripps Clinic and Research Foundation, La Jolla, CA, I joined Genentech, Inc., South San Francisco, CA in 1987. I am currently a Senior Scientist at the Department of Immunology/Discovery Research of Genentech, Inc.

3. My scientific Curriculum Vitae is attached to and forms part of this Declaration.

4. I am familiar with the Mixed Lymphocyte Reaction (MLR) assay, which has been used by me and others under my supervision, to test the immune stimulatory or immune inhibitory activity of novel polypeptides discovered in Genentech's Secreted Protein Discovery Initiative project.

5. The MLR assay is a well known and widely used proliferative assay of T-cell function, the basic protocols of which are described, for example, in Current Protocols in Immunology Vol. 1, Richard Coico, Series Ed., JohnWiley & Sons, Inc., 1991, Unit 3.12. (Exhibit A). This publication is incorporated by reference in the description of the MLR protocol in the present application.

6. The T-lymphocytes or "T-cells" of our immune system can be induced to proliferate by a variety of agents. The MLR assay is designed to study a particularly important induction mechanism whereby responsive T-cells are cultured together (or "mixed"), with other lymphocytes that are "allogeneic", e.g. lymphocytes that are taken from different individuals of the same species. In the MLR protocol of the present application, a suspension of PBMCs that includes responder T-cells, is cultured with allogeneic PBMCs that predominantly contain dendritic cells. According to the protocol, the allogeneic "stimulator" PBMCs are irradiated at a dose of 3000 Rad. This irradiation is done in order to create a sample of cells that has mainly dendritic cells. It is known that the dendritic cell population among the PBMCs are differentially affected by irradiation. At low doses (500-1000 Rad), the proliferation of most cells, including the B cells in the PBMCs, is preserved, however, at doses above 2000 Rad, this function of B cells is abolished. Dendritic cells on the other hand, maintain their antigen presentation function even at a 3000 Rad dose of radiation. (See, e.g. Current Protocols in Immunology, *supra*, at 3.12.9). Accordingly, under the conditions of the MLR assay used to test the PRO polypeptides of the present invention, the stimulator PBMCs remaining after irradiation are essentially dendritic cells.

7. Dendritic cells are the most potent antigen-presenting cells, which are able to "prime" naive T cells *in vivo*. They carry on their surface high levels of major histocompatibility complex (MHC) products, the primary antigens for stimulating T-cell proliferation. Dendritic cells provide the T-cells with potent and needed accessory or costimulatory substances, in addition to giving them the T-cell maturing antigenic signal to begin proliferation and carry out their function. Once activated by dendritic cells, the T-cells are capable of interacting with other antigen presenting B cells and macrophages to produce additional immune responses from these cells. For further details about the properties and role of dendritic cells in immune-based therapies see, e.g. Steinman, Drug News Perspect. 13(10):581-586 (Exhibit B).

8. The MLR assay of the present application is designed to measure the ability of a test substance to "drive" the dendritic cells to induce the proliferation of T-cells that are activated, or co-stimulated in the MLR, and thus identifies immune stimulants that can boost the immune system to respond to a particular antigen that may not have been immunologically active previously.

9. Such immune stimulants find important clinical applications. For example, IL-12 is a known immune stimulant, which has been shown to stimulate T-cell proliferation in the MLR assay. IL-12 was first identified in just such an MLR [Gubler et al. PNAS 88, 4143 (1991) (Exhibit C)]. In a recent cancer vaccine trial, researchers from the University of Chicago and Genetics Institute (Cambridge, MA) have demonstrated the efficacy of the approach, relying on the immune stimulatory activity of IL-12, for the treatment of melanoma. [Peterson et al. Journal of Clinical Oncology 21 (12). 2342-48 (2003) (Exhibit D)] They extracted circulating white blood cells carrying one or more markers of melanoma cells, isolated the antigen, and returned them to the patients. Normally patients would not have an immune response to his or her own human antigens. The patients were then treated with different doses of IL-12, an immune stimulant capable of inducing the proliferation of T cells that have been co-stimulated by dendritic cells. Due to the immune stimulatory effect of IL-12, the treatment provided superior results in comparison to earlier work, where patients' own dendritic cells were prepared from peripheral blood mononuclear cells (PBMCs), treated with antigens, then cultured *in vitro* and returned to the patient to stimulate anti-cancer response. [Thurner et al. J. Exp. Med. 190 (11), 1669-78 (1999) (Exhibit E)].

10. It is my considered scientific opinion that a PRO polypeptide shown to stimulate T-cell proliferation in the MLR assay of the present invention with an activity at least 180% of the control, as specified in the present application, is expected to have the type of activity as that exhibited by IL-12, and would therefore find practical utility as an immune stimulant. Some PRO polypeptides do the reverse, and give inhibition of T-cell proliferation in the MLR assay. It is my considered scientific opinion that a PRO polypeptide shown to inhibit T-cell proliferation in the MLR assay where the activity is observed as 80% or less of the control, as specified in the present application, would be expected to find practical utility when an inhibition of the immune response is desired, such as in autoimmune diseases.

Dated: 6/16/04

By: Sherman Fong

Sherman Fong, Ph.D.

2041362

Sherman Fong, Ph.D.

Senior Scientist
Department of Immunology
Genentech Inc.
1 DNA Way.
South San Francisco, California 94080-4990

19 Basinside Way
Alameda, California 94502

Work Telephone: (650) 225-2783
Home Telephone: (510) 522-5411

FAX: (650) 225-8221

Education:

1978 - 1980 Postdoctoral Fellow in Immunology, Scripps Clinic and Research Foundation, La Jolla, California

1975 - 1978 Postdoctoral Fellow in Immunology, University of California at San Francisco, San Franciso, California

1970 - 1975 Ph.D. in Microbiology, University of California at Davis, California

1966 - 1970 B.A. in Biology/Microbiology, San Francisco State University, San Francisco, California

Professional Positions:

Currently: Senior Scientist, Department of Immunology/Discovery Research, Genentech, Inc., South San Francisco, California

8/00-8/01 Acting Director, Department of Immunology, Genentech, Inc. South San Francisco, California

10/89 Senior Scientist in the Department of Immunology/Discovery Research, Genentech, Inc. South San Francisco, California

3/89 - 10/89 Senior Scientist and Immunobiology Group Leader, Department of Pharmacological Sciences, Immunobiology Section/Medical Research and Development, Genentech, Inc., S. San Francisco, California

9/87 - 3/89 Scientist, Department of Pharmacological Sciences, Immunopharmacology Section/Medical Research and Development, Genentech, Inc., S. San Francisco, California

1/82 - 9/87 Assistant Member (eq. Assistant Professor level), Department of Basic and Clinical Research, Division of Clinical Immunology, Scripps Clinic and Research Foundation, La Jolla, California

6/80 - 12/81 Scientific Associate in the Department of Clinical Research, Division of Clinical Immunology, Scripps Clinic and Research Foundation, La Jolla, California

7/78 - 6/80 Postdoctoral training in the laboratory of Dr. J. H. Vaughan, Chairman, Department of Clinical Research, Division of Clinical Immunology, Scripps Clinic and Research Foundation, La Jolla, California

2/75 - 6/78 Postdoctoral training in the laboratory of Dr. J. W. Goodman, Department of Microbiology and Immunology, School of Medicine, University of California, San Francisco, California

7/71 - 12/74 Research Assistant and Graduate Student, Department of Medical Microbiology, School of Medicine, University of California, Davis, California, under Dr. E. Benjamini

Awards:
Recipient: National Institutes of Health Postdoctoral Fellowship Award (1975).

Recipient: Special Research Award, (New Investigator Award), National Institute of Health (1980).

Recipient: P.I., Research Grant Award, National Institute of Health (1984).

Recipient: Research Career Development Award (R01), National Institutes of Health (1985).

Recipient: P.I., Multi-Purpose Arthritis Center Resarch Grant, NIH (1985)

Recipient: P.I., Resarch Grant Award, (R01 Renewal), National Institute of Health (1987).

Scientific Associations:

Sigma Xi, University of California, Davis, California Chapter

Member, The American Association of Immunologists

Committee Service and Professional Activities:

Member of the Immunological Sciences Study Section, National Institutes of Health Research Grant Review Commitee, (1988-1992).

Advisory Committee, Scientific Review Committee for Veteran's Administration High Priority Program on Aging, 1983.

Ad Hoc member of Immunological Sciences Study Section, National Institutes of Health, 1988.

Ad Hoc Reviewer: Journal of Clinical Investigations, Journal of Immunology, Arthritis and Rheumatism, International Immunology, Molecular Cell Biology, and Gastroenterology

Biotechnology Experience

Established at Genentech in 1987-1989 within the Immunobiology Laboratory, in the Department of Pharmcological Sciences, group to study the immunogenicity of recombinant hGH (Protropin®) in hGH transgenic mice.

Served as Immunologist on the **Biochemical Subteam for Protropin® Project** team.

Served as Immunologist on the **Met-less hGH and Dnase project teams**, two FDA approved biological drugs: second generation hGH Nutropin® and Pulmozyme® (DNase).

Served immunologist in1989-1990 on the **CD4-IgG project team** carrying out in vitro immunopharmacological studies of the effects of CD4-IgG on the in vitro human immune responses to mitogens and antigens and on neutrophil responses in support of the filing of IND to FDA in 1990 for use of CD4-IgG in the prevention of HIV infection. Product was dropped.

In 1989-1991, initiated and carried research and development work on antibodies to CD11b and CD18 chains of the leukocyte β2 integrins. Provided preclinical scientific data to **Anti-CD18 project team**

supporting the advancement of humanized anti-CD18 antibody as anti-inflammatory in the acute setting. IND filed in 1996 and currently under clinical evaluation.

1993-1997, **Research Project Team leader** for small molecule α4β1 integrin antagonist project. Leader for collaborative multidisciplinary team (N=11) composed of immunologists, molecular/cell biologists, protein engineers, pathologists, medicinal chemists, pharmacologists, pharmaceutical chemists, and clinical scientists targeting immune-mediated chronic inflammatory diseases. Responsible for research project plans and execution of strategy to identify lead molecules, assessment of biological activities, preclinical evaluation in experimental animals, and identification of potential clinical targets. Responsible for identification, hiring, and working with outside scientific consultants for project. Helped established and responsible for maintaining current research collaboration with Roche-Nutley. Project transfered to Roche-Nutley.

1998-present, worked with Business Development to identify and create joint development opportunity with LeukoSite (currently Millennium) for monoclonal antibody against α4β7 intergin (LDP-02) for therapeutic treatment for inflammatory bowel disease (UC and Crohn';s disease). Currently, working as scientific advisor to the core team for phase II clinical trials for LDP-02.

Currently, **Research Project Team Biology Leader** (1996-present) for small molecule antagonists for α4β7/MAdCAM-1 targeting the treatment of human inflammatory bowel diseases and diseases of the gastrointestinal tract. Responsible for leading collaborative team (N=12) from Departments of Immunology, Pathology, Analytical Technology, Antibody Technology, and Bio-Organic Chemistry to identify and evaluate lead drug candidates for the treatment of gastrointestinal inflammatory diseases.

Served for nearly fifteen years as **Ad Hoc reveiwer** on Genentech Internal Research Review Committee, Product Development Review Committee, and Pharmacological Sciences Review Committee.

Worked as Scientific advisor with staff of the **Business Development** Office on numerous occasions at Genentech, Inc. to evaluate the science of potential in-licensing of novel technologies and products.

2000-2001 Served as Research Discovery representative on Genentech Therapeutic Area Teams (Immunology/Endocrine, Pulmonary/Respiratory Disease Task Force)

Invited Symposium Lectures:

Session Chairperson and speaker, American Aging Association 12th Annual National Meeting, San Francisco, California, 1982..

Invited Lecturer, International Symposium, Mediators of Immune Regulation and Immunotherapy, University of Western Ontario, London, Ontario, Canada, 1985.

Invited Lecturer, workshop on Human IgG Subclasses, Rheumatoid Factors, and Complement. American Association of Clinical Chemistry, San Francisco, California, 1987.

Plenary Lecturer, First International Waaler Conference on Rheumatoid Factors, Bergen, Norway, 1987.

Invited Lecturer, Course in Immunorheumatology at the Universite aux Marseilles, Marseilles, France, 1988.

Plenary Lecturer, 5th Mediterranean Congress of Rheumatology, Istanbul, Turkey, 1988.

Invited Lecturer, Second Annual meeting of the Society of Chinese Bioscientist of America, University of California, Berkeley, California, 1988.

Lecturer at the inaugural meeting of the Immunology by the Bay sponsored by The Bay Area Bioscience Center. The β2 Integrins in Acute Inflammation, July 14, 1992.

Lecturer, "Research and Development -- An Anatomy of a Biotechnology Company", University of California, Berkeley, Extension Course, given twice a year--March 9, 1995 to June 24, 1997.

Lecturer, "The Drug Development Process – Biologic Research - Genomics", University of California, Berkeley Extension, April 21, 1999, October, 1999, April 2000, October, 2000.

Lecturer, "The Drug Development Process – Future Trends/Impact of Pharmacogenomics", University of California Berkeley Extension, April 2001, October 2001, April 2002.

Invited Speaker, "Targeting of Lymphocyte Integrin α4β7 Attentuates Inflammatory Bowel Diseases", in Sympoium on "Nutrient effects on Gene Expression" at the Institute of Food Technology Symposium, June, 2002.

Patents:
Dennis A. Carson, Sherman Fong, Pojen P. Chen.
U.S. Patent Number 5,068,177: Anti-idiotype Antibodies induced by Synthetic Polypeptides, Nov. 26, 1991

Sherman Fong, Caroline A. Hebert, Kyung Jin Kim and Steven R. Leong.
U.S. Patent Number 5,677,426: Anti-IL-8 Antibody Fragments, Oct. 14, 1997

Claire M. Doerschuk, Sherman Fong, Caroline A. Hebert, Kyung Jin Kim, Steven R. Leong. U.S. Patent Number 5,686,070: Methods for Treating Bacterial Pneumonia, Nov. 11, 1997

Claire M. Doerschuk, Sherman Fong, Caroline A. Hebert, Kyung Jin Kim, Steven R. Leong. U.S. Patent 5,702,946: Anti-IL-8 Monoclonal Antibodies for the Treatment of Inflammatory Disorders, Dec. 30, 1997

Sherman Fong, Caroline A. Hebert, Kyung Jin Kim, Steven R. Leong.
U.S. Patent Number 5,707,622: Methods for Treating Ulcerative Colits, Jan. 13, 1998

Sherman Fong, Napoleone Ferrara, Audrey Goddard, Paul Godowski, Austin Gurney, Kenneth Hillan, and Mickey Williams. U.S. Patent Number 6,074,873: Nucleic acids encoding NL-3, June 13, 2000

Sherman Fong, Napoleone Ferrara, Audrey Goddard, Paul Godowski, Austin Gurney, Kenneth Hillan, and Mickey Williams. U.S. Patent Number 6,348,351 B1: The Receptor Tyrosine Kinase Ligand Homologues. February 19, 2002

Patent Applications:

Sherman Fong, Kenneth Hillan, Toni Klassen
U.S. Patent Application: "Diagnosis and Treatment of Hepatic Disorders"

Sherman Fong, Audrey Goddard, Austin Gurney, Daniel Tumas, William Wood
U.S. Patent Application: Compositions and Methods for the Treatment of Immune Related Diseases.

Sherman Fong, Mary Gerritsen, Audrey Goddard, Austin Gurney, Kenneth Hillan, Mickey Williams, William Wood . U.S. Patent Application: Promotion or Inhibition of Cardiovasculogenesis and Angiogenesis

Avi Ashkenazi, Sherman Fong, Audrey Goddard, Austin Gurney, Mary Napier, Daniel Tumas, William Wood. US Patent Application: Compounds, Compositions and Methods for the Treatment of Diseases Characterized by A33-Related Antigens

Chen, Filvaroff, Fong, Goddard, Godowski, Grimaldi, Gurney, Hillan, Tumas, Vandlen, Van Lookeren, Watanabe, Williams, Wood, Yansura
US Patent Application: IL-17 Homologous Polypeptides and Therapeutic Uses Thereof

Ashkenazi, Botstein, Desnoyers, Eaton, Ferrara, Filvaroff, Fong, Gao, Gerber, Gerritsen, Goddard, Godowski, Grimaldi, Gurney, Hillan, Kljavin, Mather, Pan, Paoni, Roy, Stewart, Tumas, Williams, Wood
US Patent Application: Secreted And Transmembrane Polypeptides And Nucleic Acids Encoding The Same

Publications:

1. Scibienski R, Fong S, Benjamini E: Cross tolerance between serologically non-cross reacting forms of egg white lysozyme. J Exp Med 136:1308-1312, 1972.

2. Scibienski R, Harris M, Fong S, Benjamini E: Active and inactive states of immunological unresponsiveness. J Immunol 113:45-50, 1974.

3. Fong S: Studies on the relationship between the immune response and tumor growth. Ph D Thesis, 1975.

4. Benjamini E, Theilen G, Torten M, Fong S, Crow S, Henness AM: Tumor vaccines for immunotherapy of canine lymphosarcoma. Ann NY Acad Sci 277:305, 1976.

5. Benjamini E, Fong S, Erickson C, Leung CY, Rennick D, Scibienski RJ: Immunity to lymphoid tumors induced in syngeneic mice by immunization with mitomycin C treated cells. J Immunol 118:685-693, 1977.

6. Goodman JW, Fong S, Lewis GK, Kamin R, Nitecki DE, Der Balian G: T lymphocyte activation by immunogenic determinants. Adv Exp Biol Med 98:143, 1978.

7. Goodman JW, Fong S, Lewis GK, Kamin R, Nitecki DE, Der Balian G: Antigen structure and lymphocyte activation. Immunol Rev 39:36, 1978.

8. Fong S, Nitecki DE, Cook RM, Goodman JW: Spatial requirements of haptenic and carrier determinants for T-dependent antibody responses. J Exp Med 148:817, 1978.

9. Fong S, Chen PP, Nitecki DE, Goodman JW: Macrophage-T cell interaction mediated by immunogenic and nonimmunogenic forms of a monofunctional antigen. Mol Cell Biochem 25:131, 1979.

10. Tsoukas CD, Carson DA, Fong S, Pasquali J-L, Vaughan JH: Cellular requirements for pokeweed mitogen induced autoantibody production in rheumatoid arthritis. J Immunol 125:1125-1129, 1980.

11. Pasquali J-L, Fong S, Tsoukas CD, Vaughan JH, Carson DA: Inheritance of IgM rheumatoid factor idiotypes. J Clin Invest 66:863-866, 1980.

12. Fong S, Pasquali J-L, Tsoukas CD, Vaughan JH, Carson DA: Age-related restriction of the light chain heterogeneity of anti-IgG antibodies induced by Epstein-Barr virus stimulation of human lymphocytes in vitro. Clin Immunol Immunopathol 18:344, 1981.

13. Fong S, Tsoukas CD, Frincke LA, Lawrance SK, Holbrook TL, Vaughan JH, Carson DA: Age-associated changes in Epstein-Barr virus induced human lymphocyte autoantibody responses. J Immunol 126:910-914, 1981.

14. Tsoukas CD, Fox RI, Slovin SF, Carson DA, Pellegrino M, Fong S, Pasquali J-L, Ferrone S, Kung P, Vaughan JH: T lymphocyte-mediated cytotoxicity against autologous EBV-genome-bearing B cells. J Immunol 126:1742-1746, 1981.

15. Fong S, Tsoukas CD, Pasquali J-L, Fox RI, Rose JE, Raiklen D, Carson DA, Vaughan JH: Fractionation of human lymphocyte subpopulations on immunoglobulin coated petri dishes. J Immunol Methods 44:171-182, 1981.

16. Pasquali J-L, Tsoukas CD, Fong S, Carson DA, Vaughan JH: Effect of Levamisole on pokeweed mitogen stimulation of immunoglobulin production in vitro. Immunopharmacology 3:289-298, 1981.

17. Pasquali J-L, Fong S, Tsoukas CD, Hench PK, Vaughan JH, Carson DA: Selective lymphocyte deficiency in seronegative rheumatoid arthritis. Arthritis Rheum 24:770-773, 1981.

18. Fong S, Fox RI, Rose JE, Liu J, Tsoukas CD, Carson DA, Vaughan JH: Solid- phase selection of human T lymphocyte subpopulations using monoclonal antibodies. J Immunol Methods 46:153-163, 1981.

19. Pasquali J-L, Fong S, Tsoukas CD, Slovin SF, Vaughan JH, Carson DA: Different populations of rheumatoid factor idiotypes induced by two polyclonal B cell activators, pokeweed mitogen and Epstein-Barr virus. Clin Immunol Immunopathol 21:184-189, 1981.

20. Carson DA, Pasquali J-L, Tsoukas CD, Fong S, Slovin SF, Lawrance SK, Slaughter L, Vaughan JH: Physiology and pathology of rheumatoid factors. Springer Semin Immunopathol 4:161-179, 1981.

21. Fox RI, Fong S, Sabharwal N, Carstens SA, Kung PC, Vaughan JH: Synovial fluid lymphocytes differ from peripheral blood lymphocytes in patients with rheumatoid arthritis. J Immunol 128:351-354, 1982.

22. Seybold M, Tsoukas CD, Lindstrom J, Fong S, Vaughan JH: Acetylcholine receptor antibody production during leukoplasmapheresis for Myasthenia Gravis. Arch Neurol 39:433-435, 1982.

23. Tsoukas CD, Fox RI, Carson DA, Fong S, Vaughan JH: Molecular interactions in human T-cell-mediated cytotoxicity to Epstein-Barr virus. I. Blocking of effector cell function by monoclonal antibody OKT3. Cell Immunol 69:113-121, 1982.

24. Sabharwal UK, Vaughan JH, Fong S, Bennett P, Carson DA, Curd JG: Activation of the classical pathway of complement by rheumatoid factors: Assessment by radioimmunoassay for C4. Arthritis Rheum 25:161-167, 1982.

25. Fox RI, Carstens SA, Fong S, Robinson CA, Howell F, Vaughan JH: Use of monoclonal antibodies to analyze peripheral blood and salivary gland lymphocyte subsets in Sjogren's Syndrome. Arthritis Rheum 25:419, 1982.

26. Fong S, Miller JJIII, Moore TL, Tsoukas CD, Vaughan JH, Carson DA: Frequencies of Epstein-Barr virus inducible IgM anti-IgG B lymphocytes in normal children and in children with Juvenile Rheumatoid Arthritis. Arthritis Rheum 25:959-965, 1982.

27. Goodman JW, Nitecki DE, Fong S, Kaymakcalan Z: Antigen bridging in the interaction of T helper cells and B cells. Adv Exp Med Biol 150:219-225, 1982.

28. Goodman JW, Nitecki DE, Fong S, Kaymakcalan Z: Antigen bridging in T cell-B cell interaction: Facts or fiction. In: Protein Conformation as Immunologic Signal. EMBO Workshop, Portonenere, Italy, 1982.

29. Tsoukas CD, Carson DA, Fong S, Slovin SF, Fox RI, Vaughan JH: Lysis of autologous Epstein-Barr virus infected B cells by cytotoxic T lymphocytes of rheumatoid arthritis patients. Clin Immunol Immunopathol 24:8-14, 1982.

30. Fong S, Vaughan JH, Tsoukas CD, Carson DA: Selective induction of autoantibody secretion in human bone marrow by Epstein-Barr virus. J Immunol 129:1941-1945, 1982.

31. Sabharwal UK, Fong S, Hoch S, Cook RD, Vaughan JH, Curd JG: Complement activation by antibodies to Sm in systemic lupus erythematosus. Clin Exp Immunol 51:317-324, 1983.

32. Tsoukas CD, Carson DA, Fong S, Vaughan JH: Molecular interactions in human T cell mediated cytotoxicity to EBV. II. Monoclonal antibody OKT3 inhibits a post-killer-target recognition/adhesion step. J Immunol 129:1421-1425, 1982.

33. Welch MJ, Fong S, Vaughan JH, Carson DA: Increased frequency of rheumatoid factor precursor B lymphocytes after immunization of normal adults with tetanus toxoid. Clin Exp Immunol 51:299-305, 1983.

34. Fong S, Vaughan JH, Carson DA: Two different rheumatoid-factor producing cell populations distinguished by the mouse erythrocyte receptor and responsiveness to polyclonal B cell activators. J Immunol 130:162-164, 1983.

35. Fox RI, Hueniken M, Fong S, Behar S, Royston I, Singhal SK, Thompson L: A novel cell surface antigen (T305) found in increased frequency on acute leukemia cells and in autoimmune disease states. J Immunol 131:762-767, 1983.

36. Fong S: Solid-phase panning for the fractionation of lymphoid cells. In: Cell separation: methods and selected applications. Pretlow TG, Pretlow TP (eds.) pp. 203-219. Academic Press, New York, 1983.

37. Carson DA, Fong S: A common idiotype on human rheumatoid factors identified by a hybridoma antibody. Mol Immunol 20:1081-1087, 1983.

38. Fong S, Gilbertson TA, Carson DA: The internal image of IgG in cross- reactive anti-idiotypic antibodies against human rheumatoid factors. J Immunol 131:719-724, 1983.

39. Fox RI, Adamson TC, Fong S, Young C, Howell FV: Characterization of the phenotype and function of lymphocytes infiltrating the salivary gland in patients with primary Sjogren syndrome. Diagn Immunol 1:233-239, 1983.

40. Fox RI, Adamson III TC, Fong S, Robinson CA, Morgan EL, Robb JA, Howell FV: Lymphocyte phenotype and function in pseudolymphoma associated with Sjogren's syndrome. J Clin Invest 72:52-62, 1983.

41. Fong S, Gilbertson TA, Chen PP, Vaughan JH, Carson DA: Modulation of human rheumatoid factor-specific lymphocyte responses with a cross- reactive anti-idiotype bearing the internal image of antigen. J Immunol 132:1183-1189, 1984.

42. Chen PP, Houghten RA, Fong S, Rhodes GH, Gilbertson TA, Vaughan JH, Lerner RA, Carson DA: Anti-hypervariable region antibody induced by a defined peptide. A new approach for studying the structural correlates of idiotypes. Proc Natl Acad Sci USA 81:1784-1788, 1984.

43. Fox RI, Fong S, Tsoukas CD, Vaughan JH: Characterization of recirculating lymphocytes in rheumatoid arthritis patients: Selective deficiency of natural killer cells in thoracic duct lymph. J Immunol 132:2883-2887, 1984.

44. Chen PP, Fong S, Normansell D, Houghten RA, Karras JG, Vaughan JH, Carson DA: Delineation of a cross-reactive idiotype on human autoantibodies with antibody against a synthetic peptide. J Exp Med 159:1502-1511, 1984.

45. Fong S, Carson DA, Vaughan JH: Rheumatoid factor. In: Immunology of Rheumatic Diseases. Gupta S, Talal N (eds.): Chapter 6. pp. 167-196. Plenum Publishing Corp., New York, 1985.

46. Fong S: Immunochemistry. In: Immunology as applied to Otolaryngology. Ryan AF, Poliquis JF, Harris A (eds.): pp. 23-53. College Hill Press, San Diego, 1985.

47. Fong S, Chen PP, Vaughan JH, Carson DA: Origin and age-associated changes in the expression of a physiologic autoantibody. Gerontology 31:236-250, 1985.

48. Chen PP, Fong S, Houghten RA, Carson DA: Characterization of an epibody: An anti-idiotype which reacts with both the idiotype of rheumatoid factors (RF) and the antigen recognized by RFs. J Exp Med 161:323, 1985.

49. Chen PP, Goni F, Fong S, Jirik F, Vaughan JH, Frangione B, Carson DA: The majority of human monoclonal IgM rheumatoid factors express a primary structure-dependent cross-reactive idiotype. J Immunol 134:3281-3285, 1985.

50. Lotz M, Tsoukas CD, Fong S, Carson DA, Vaughan JH: Regulation of Epstein- Barr virus infections by recombinant interferon. Selected sensitivity to interferon-gamma. Eur J Immunol 15:520-525, 1985.

51. Chen PP, Kabat EA, Wu TT, Fong S, Carson DA: Possible involvement of human D-minigenes in the first complementarity-determining region of kappa light chains. Proc Natl Acad Sci USA 82:2125-2127, 1985.

52. Goldfien RD, Chen PP, Fong S, Carson DA: Synthetic peptides corresponding to third hypervariable region of human monoclonal IgM rheumatoid factor heavy chains define an immunodominant idiotype. J Exp Med 162:756-761, 1985.

53. Fong S, Chen PP, Gilbertson TA, Fox RI, Vaughan JH, Carson DA: Structural similarities in the kappa light chains of human rheumatoid factor paraproteins and serum immunoglobulins bearing a cross-reactive idiotype. J Immunol 135:1955-1960, 1985.

54. Chen PP, Goni F, Houghten RA, Fong S, Goldfien RD, Vaughan JH, Frangione B, Carson DA: Characterization of human rheumatoid factors with seven antiidiotypes induced by synthetic hypervariable-region peptides. J Exp Med 162:487-500, 1985.

55. Fong S, Gilbertson TA, Hueniken RJ, Singhal SK, Vaughan JH, Carson DA: IgM rheumatoid factor autoantibody and immunoglobulin producing precursor cells in the bone marrow of humans. Cell Immunol 95:157-172, 1985.

56. Fong S, Chen PP, Goldfien RD, Jirik F, Silverman G, Carson DA: Recurrent idiotypes of human anti-IgG autoantibodies: their potential use for immunotherapy. In: Mediators of Immune Regulation and Immunotherapy. Singhal SK, Delovitch TL (eds.): pp. 232-243. Elsevier Science Publishing Co., New York, 1986.

57. Fox RI, Chen PP, Carson DA, Fong S: Expression of a cross reactive idiotype on rheumatoid factor in patients with Sjogren's syndrome. J Immunol 136:477-483, 1986.

58. Jirik FR, Sorge J, Fong S, Heitzmann JG, Curd JG, Chen PP, Goldfien R, Carson DA: Cloning and sequence determination of a human rheumatoid factor light-chain gene. Proc Natl Acad Sci USA, 83:2195-2199, 1986.

59. Lotz M, Tsoukas CD, Fong S, Dinarello CA, Carson DA, Vaughan JH: Release of lymphokines following Epstein-Barr virus infection in vitro. I. The sources and kinetics of production of interferons and interleukins in normal humans. J Immunol, 136:3636-3642, 1986.

60. Lotz M, Tsoukas CD, Fong S, Dinarello CA, Carson DA, Vaughan JH: Release of lymphokines following infection with Epstein-Barr virus in vitro. II. A monocyte dependent inhibitor of interleukin-1 downregulates the production of interleukin-2 and gamma interferon in rheumatoid arthritis. J Immunol, 136:3643-3648, 1986.

61. Fong S, Chen PP, Gilbertson TA, Weber JR, Fox RI, Carson DA: Expression of three cross reactive idiotypes on rheumatoid factor autoantibodies from patients with autoimmune diseases and seropositive adults. J Immunol, 137:122-128, 1986.

62. Fong S, Gilbertson TA, Chen PP, Karras JG, Vaughan JH, Carson DA: The common occurrence of internal image type anti-idiotypic antibodies in rabbits immunized with monoclonal and polyclonal human IgM rheumatoid factors. Clin Exp Immunol, 64:570-580, 1986.

63. Fox RI, Carson DA, Chen P, Fong S: Characterization of a cross reactive idiotype in Sjogren's syndrome. Scand J Rheum S61:83-88, 1986.

64. Silverman GJ, Carson DA, Solomon A, Fong S: Human kappa light chain subgroup analysis with synthetic peptide-induced antisera. J Immunol Methods 95:249-257, 1987.

65. Goldfien R, Chen P, Kipps TJ, Starkebaum G, Heitzmann JG, Radoux V, Fong S, Carson DA: Genetic analysis of human B cell hybridomas expressing a rheumatoid factor-associated cross-reactive idiotype. J Immunol 138:940- 944, 1987.

66. Carson DA, Chen PP, Fox RI, Kipps TJ, Jirik F, Goldfien RD, Silverman G, Radoux V, Fong S: Rheumatoid factors and immune networks. Annu Rev Immunol 5:109-126, 1987.

67. Kipps TJ, Fong S, Tomhave E, Chen PP, Goldfien RD, Carson DA: High frequency expression of a conserved kappa variable region gene in chronic lymphocytic leukemia. Proc Natl Acad Sci USA 84:2916-2920, 1987

68. Fong S, Chen PP, Fox RI, Goldfien RD, Silverman GJ, Radoux V, Jirik F, Vaughan JH, Carson DA: Rheumatoid factors in human autoimmune disease: Their origin, development and function. Path Immunopath Res 5:407-449, 1987.

69. Goldfien RD, Fong S, Chen P, Carson DA: Structure and function of rheumatoid factor: Implications for its role in the pathogenesis of mixed cryoglobulinemia. In: Antiglobulins, cryoglobulins and glomerulonephritis, Proceedings of 2nd International Milano Meeting of Nephrology. Ponticelli C, Minetti L, D'Amico G (eds.) Martinus Nijhoff, Dordrecht pp. 17-27, 1986.

70. Silverman GJ, Carson DA, Patrick K, Vaughan JH, Fong S: Expression of a germline human kappa chain associated cross reactive idiotype after in vitro and in vivo infection with Epstein-Barr virus. Clin Immunol Immunopathol 43:403-411, 1987.

71. Silverman GJ, Fong S, Chen PP, Carson DA: Clinical update: Cross reactive idiotype and the genetic origin of rheumatoid factors. J Clin Lab Anal, 1:129-135, 1987.

72. Chen PP, Fong S, Carson DA: Molecular basis of reactivity of epibodies. In: Elicitation and use of anti-idiotypic antibodies and their biological applications. Bona C (ed.), CRC Press, Boca Raton, Fla, in press.

73. Fong S, Chen PP, Carson DA, Fox, RI: Rheumatoid factor in Sjogren's syndrome. In: Sjogren's Syndrome: Clinical and Immunological Aspects. Talal N, Moutsopoulos HM, Kassan SS (eds.), Springer-Verlag, New York, pp. 203-217, 1987.

74. Chen PP, Fong S, Carson DA: The use of defined peptides in characterizing idiotypes. Int Rev Immunol 2:419-432, 1987.

75. Chen PP, Fong S, Goni F, Houghten RA, Frangione B, Liu F, Carson DA: Analyses of human rheumatoid factors with anti-idiotypes induced by synthetic peptides. Monogr Allergy 22:12-23, 1987.

76. Carson DA, Chen PP, Radoux V, Jirik F, Goldfien RD, Silverman GJ, Fong S: Molecular basis for the cross-reactive idiotypes on human anti-IgG autoantibodies (rheumatoid factors) In: Autoimmunity and Autoimmune Disease. Ciba Foundation Symposium 129 pp. 123-130, 1987.

77. Radoux V, Fong S, Chen PP, Carson DA: Rheumatoid factors: current concepts. In: Advances in Inflammation Research. Lewis, A. (Ed), Raven Press, New York, pp.295-304, 1987.

78. Kipps TJ, Fong S, Chen PP, Miller WE, Piro LD, Carson DA: Immunoglobulin V gene utilization in CLL. In: Chronic lymphocytic leukemia: recent progress and future direction, Alan R Liss, Inc., New York, pp. 115-126, 1987.

79. Fong S, Chen PP, Fox RI, Goldfien RD, Radoux V, Silverman GJ, Crowley JJ, Roudier J, Carson DA: The diversity and idiotypic pattern of human rheumatoid factors in disease. Concepts in Immunopath 5: 168-191, 1988.

80. Fox RI, Fong S, Chen PP, Kipps TJ: Autoantibody production in Sjogren's syndrome: a hypothesis regarding defects in somatic diversification of germline encoded genes. In Vivo 2: 47-56, 1988.

81. Chen PP, Fong S, Goni F, Silverman GJ, Fox RI, Liu M-K, Frangione B, Carson DA: Cross-reacting idiotypes on cryoprecipitating rheumatoid factor. Springer Seminar Series in Immunopath 10: 35-55, 1988.

82. Chen PP, Fong S, Carson DA: Rheumatoid factor. Rheumatic Diseases of North America 13:545-568, 1987.

83. Carson DA, Chen PP, Kipps TJ, Radoux V, Jirik FR, Goldfien RD, Fox RI, Silverman GJ, Fong S. Idioytpic and genetic studies of human rheumatoid factors. Arthritis Rheum 30: 1321-1325, 1987.

84. Fong S, Chen PP, Crowley JJ, Silverman GJ, Carson DA: Idiotypic characteristics of rheumatoid factors. Scand J Rheumatol, Suppl. 75: 58-65, 1988.

85. Crowley JJ, Goldfien RD, Schrohenloher RE, Spiegelberg HL, Silverman GJ, Mageed RA, Jefferis R, Koopman WJ, Carson DA, Fong S: Incidence of three cross reactive idiotypes on human rheumatoid factor paraproteins. J Immunol 140: 3411-3418, 1988.

86. Fong S, Chen PP, Crowley JJ, Silverman GJ, Carson DA: Idiotypes and the structural diversity of human rheumatoid factors. Springer Seminar Series in Immunopath 10: 189-201, 1988.

87. Silverman GJ, Goldfien, Chen PP, Mageed RA, Jefferis R, Goni F, Frangione B, Fong S, Carson DA. Idiotypic and subgroup analysis of human monoclonal rheumatoid factors: implications for structural and genetic basis of autoantibodies in humans. J Clin Invest 82: 469-475, 1988.

88. Fox RI, Chan E, Benton L, Fong S, Friedlander M. Treatment of primary Sjogren' syndrome with hydroxychloroquine. American Journal of Medicine 85 (suppl 4A): 62-67, 1988.

89. Fong S. La Diversite Structurale Des Facteurs Rhumatoides Humains. In Immunorhumatologie. Roux H, Luxembourg A, Roudier J, (Eds.). Solal, editeurs, Marseille, pp 162-166, 1989.

90. Fu, Y., Arkin, S., Fuh, G., Cunningham, B.C., Wells, J.A., Fong, S., Cronin, M., Dantzer, R., Kelley, K. Growth hormone augments superoxide anion secretion of human neutrophils by binding to the prolactin receptor. J. Clin. Invest 89: 451-457, 1992.

91. Weber, J.R., Nelson, C., Cunningham, B.C., Wells, J.A., Fong, S. Immunodominant structures of human growth hormone identified by homolog-scanning mutagenesis. Mol. Immunol. 29: 1081-1088, 1992.

92. Bushell, G., Nelson, C., Chiu, H., Grimley, C., Henzel, W., Burnier, J., Fong, S. The role of cathepsin B in the generation of T cell antigenic epitopes of human growth hormone. Mol. Immunol. 30:587-591, 1993.

93. Bednarczyk, J.L., Wygant, J.N., Szabo, M.C., Molinari-Storey, L., Renz, M., Fong, S., McIntyre, B.W. Homotypic leukocyte aggregation triggered by a monoclonal antibody specific for novel epitope expressed by the integrin β1 subunit: Conversion of non-responsive cells by transferring human α4 subunit cDNA. J. Cell. Biochem. 51: 465-478, 1993.

94. Berman, P.W., Nakamura, G., Riddle, L., Chiu, H., Fisher, K., Champe, M., Gray, A., Ward, P., Fong, S. Biosynthesis and function of membrane bound and secreted forms of recombinant Mac-1. J. Cell. Biochem. 52:183-195, 1993.

95. Crowe, D.T., Chiu, H., Fong, S., Weissman, I.L. Regulation of the avidity of integrin α4β7 by the β7 cytoplasmic domain. J. Biol. Chem. 269:14411-14418, 1994.

96. Renz, M.E., Chiu, H.H., Jones, S., West, C., Fox, J., Kim, J.K., Presta, L.G., Fong, S. Structural requirements for adhesion of soluble recombinant murine VCAM-1 to α4β1. J. Cell Biol. 125:1395-1406, 1994.

97. Chiu, H. H., Crowe, D. T., Renz, M. E., Presta, L. G., Jones, S., Weissman, I. L., and Fong, S. Similar but non-identical amino acid residues on vascular cell adhesion molecule-1 are involved in the interaction with α4β1 and α4β7 under different activity states. J. Immunol. 155:5257-5267, 1995.

98. Viney, J. L., Jones, S., Chiu, H., Lagrimas, B., Renz, M., Presta, L., Jackson, D., Hillan, K., Fong, S. Mucosal Addressin Cell Adhesion Molecule-1. A structural and functional analysis demarcates the integrin binding motif. J. Immunol. 157: 2488-2497, 1996.

99. Fong, S., Jones, S., Renz, M.E., Chiu, H.H., Ryan, A.M., Presta, L. G., and Jackson, D. Mucosal Addressin Cell Adhesion Molecule-1 (MAdCAM-1)--Its binding motif for α4β7 and role in experimental colitis. Immunologic Research 16: 299-311, 1997.

100. Jackson, D.Y., Quan, C., Artis, D.R., Rawson, T., Blackburn, B., Struble, M., Fitzgerald, G., Chan K., Mullin, S., Burnier, J.P., Fairbrother, W.J., Clark, K., Beresini, M., Chiu, H., Renz, M., Jones, S., and Fong, S. Potent α4β1 Peptide Antagonists as Potential Anti-Inflammatory Agents. J. Med. Chem. 40: 3359-3368, 1997.

101. Viney, J.L. and Fong, S. β7 Integrins and Their Ligands in Lymphocyte Migration to the Gut. Chemical Immunology: 'Mucosal T Cells' . Chemical Immunology 71;64-76, 1998.

102. Bradley, L.M., Malo, M.E., Fong, S., Tonkonogy, S.L., and Watson, S.R. Blockade of both L-selectin and α4 Integrins Abrogate Naïve CD4 Cell Trafficking and Responses in Gut-Associated Lymphoid Organs. International Immunology 10, 961-968, 1998.

103. Quan, C., Skelton, N., Clark, K., Jackson, D.Y., Renz, M., Chiu, H.H., Keating, S.M., Beresini, M.H., Fong, S., and Artis D.R. Transfer of a Protein Binding Epitope to a Minimal Designed Peptide. Bioploymers (Peptide Science);47,265-275, 1998.

104. Hillan, K.J., Hagler, K.E., MacSween, R.N.M., Ryan, A.M., Renz, M.E., Chiu, H.H., Ferrier, R.K., Bird, G.L., Dhillon, A.P., Ferrell, L.D., Fong, S. Expression of the Mucosal Vascular Addressin, MAdCAM-1, in Inflammatory Liver Disease. Liver 19, 509-518, 1999

105. Pender, S.L.F., Salmela, M.T., Monteleone, G., Schnapps, D., McKenzie, C., Spencer, J., Fong, S., Saarialho-Kere, U., and MacDonald, T.T. Ligation of alpha 4 beta 1 integrin on human intestinal mucosal mesenchymal cells selectively upregulates membrane type-1 matrix metalloproteinase and confers a migratory phenotype. American Journal of Pathology 157, 1955-1962, 2000.

106. Liang, T.W., DeMarco, R., Gurney, A., Hooley, J., Huang, A., Klassen, T., Mrsny, R., Tumas, D., Wright, B.D., and Fong, S. Characterization of Human Junctional Adhesion Molecule (huJAM): Evidence for involvement in cell-cell contact and tight junction regulation. American Journal of Physiology; Cell Physiology 279, C1733-C1743, 2000.

107. Liang, T.W., Chiu, H.H., Gurney, A., Sidle, A., Tumas, D.B., Schow, P., Foster, J., Klassen, T., Dennis, K., DeMarco, RA.., Pham T., Frantz, G., Fong, S. VE-JAM/JAM 2 interacts with T, NK, and dendritic cells through JAM 3. J.Immunology 168, 1618-1626, 2002.

107. Dupree,N., Artis, D.R., Castanedo, G., Marsters, J., Sutherlin, D., Caris, L., Clark, K., Keating, S.,Beresini, M., Chiu, H., Fong, S., Lowman, H., Skeleton, N., and Jackson, D. Selective $\alpha 4\beta 7$ Antagonists and Their Potential as Anti-Inflammatory Agents. J. Med. Chem. 45, 3451-3457, 2002.

108. Castanedo, G.M., Sailes, F.C., Dubree, N., Nicholas, J., Caris, L., Keating, S., Chiu, H., Fong, S., Marsters, J., Jackson, D.Y., Sutherlin, D.P. The Solid Phase Synthesis of Dual $\alpha 4\beta 1/\alpha 4\beta 7$ Antagonists: Two Scaffolds with Overlapping Pharmacophores. Bioorganic and Medicinal Chemistry Letters 12, 2913-2917, 2002.